In the Drawing:

Please amend the drawing figures in accordance Annexure 3, attached hereto, which constitutes sketches presented on twelve (12) replacement drawing sheets annexed hereto.

REMARKS

Amendments are presented herein to improve the form of the subject application and in response to the Examiner's comments in the above-identified Office Action.

Drawings

Figures 1, 11, 12, 14, 15, 19, 20 and 22-26 are considered by the Examiner to be objectionable because the size of the figures and the font size of the legends are too small to properly and clearly review the figures and zooming into the figure is not possible due to poor resolution. The Examiner has required that Applicants provide corrected drawing sheets in compliance with 37 C.F.R. § 1.121(d) in reply to the Office action to avoid abandonment of the application.

The Examiner advises that any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. According to the Examiner, each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 C.F.R. § 1.121(d). If the changes are not accepted by the Examiner,

Applicants will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance by the Examiner.

APPLICANTS' RESPONSE

Applicants have amended the drawing figures to conform to the requirements stated by the Examiner. More specifically, the drawings have been redrawn in a larger size and all text has been replaced with higher resolution text. No new matter has been added to the drawing figures, and all REPLACEMENT SHEETS are attached and have been identified accordingly, as required by the Examiner.

The resulting distribution of the drawing figures is as follows:

Fig. 1 - Formerly on same sheet with Figs. 2a and 2b. Now, enlarged and clarified Fig. 1 is on a separate REPLACEMENT SHEET, and Figs, 2a and 2b are together on a separate REPLACEMENT SHEET;

Fig. 11 - Formerly on same sheet with Fig. 12. Now, enlarged and clarified Fig. 11 is on a separate REPLACEMENT SHEET;

Fig. 12 - Formerly on same sheet with Fig. 11. Now, enlarged and clarified Fig. 12 is on a separate REPLACEMENT SHEET;

Fig. 14 - Formerly on same sheet with Fig. 15. Now, enlarged and clarified Fig. 14 is on a separate REPLACEMENT SHEET;

Fig. 15 - Formerly on same sheet with Fig. 14. Now, enlarged and clarified Fig. 15 is on a separate REPLACEMENT SHEET;

Fig. 19 - Formerly on same sheet with Fig. 20. Now, enlarged and clarified Fig. 19 is on a separate REPLACEMENT SHEET;

Fig. 20 - Formerly on same sheet with Fig. 19. Now, enlarged and clarified Fig. 20 is on a separate REPLACEMENT SHEET;

Fig. 22 - Formerly on same sheet with Figs. 23 and 24. Now, enlarged and clarified Fig. 22 is on a separate REPLACEMENT SHEET with Fig. 23;

Fig. 23 - Formerly on same sheet with Figs. 22 and 24. Now, enlarged and clarified Fig. 23 is on a separate REPLACEMENT SHEET with Fig. 22;

Fig. 24 - Formerly on same sheet with Figs. 22 and 23. Now, enlarged and clarified Fig. 24 is on a separate REPLACEMENT SHEET;

Fig. 25 - Formerly on same sheet with Fig. 26. Now, enlarged and clarified Fig. 25 is on a separate REPLACEMENT SHEET; and

Fig. 26 - Formerly on same sheet with Fig. 25. Now, enlarged and clarified Fig. 26 is on a separate REPLACEMENT SHEET.

In view of the foregoing, it is respectfully asserted that the Examiner's objections to the drawings have been overcome.

Claim Rejections - 35 U.S.C. § 101

The Examiner states that "claims 1-10 stand rejected under 35 U.S.C. § 101 because the claimed invention is considered by the Examiner to be directed to non-statutory subject matter."

The Examiner further states that claims 1-6 stand rejected under 35 U.S.C. § 101 because the claimed invention is considered by the Examiner to be directed to non-statutory subject matter. In particular, the Examiner states that "claims 1-9 are drawn to a process." The Examiner continues the comment by noting that under 35 U.S.C. § 101 a process must 1) be tied to another statutory class (such as a particular apparatus) or 2) transform underlying subject matter (such as an article or materials) to a different state or thing. The claimed process steps are not considered by the Examiner to transform underlying subject matter.

The Examiner continues the comment by noting that to qualify as a 35 U.S.C. § 101 statutory process, the claims should positively recite the other statutory class (apparatus or thing) to which it is tied, for example by identifying the apparatus that accomplishes the method steps.

In this regard, the Examiner directs Applicants to http://www.uspto.gov/web/offices/pac/dapp/-opla/preognotice/section_101_05_15_2008.pdf.

APPLICANTS' RESPONSE

Applicants respectfully disagree with several aspects of the Examiner's comments. First it is noted that the Examiner has rejected claims 1-10 under 35 U.S.C. § 101. This rejection should not be applied to independent claim 7, which is clearly an apparatus claim, and its associated dependent claims 8-10.

Second, for the reason indicated above, Applicants disagree with the Examiner's assertion that "claims 1-9 are drawn to a process." According to Applicants' records, claims 7-10 are apparatus claims, not process claims. More specifically, independent claim 7 specifies a first memory; a second memory ; a third memory; a signal combiner arrangement; a limiter ; and a virtual anesthesia monitor. None of these claimed elements constitutes a process step.

With respect to independent claims 1 and 4, these claims have been amended to conform with the Examiner's stated requirements imposed by 35 U.S.C. § 101. The claimed process is now directed to the use of a computing machine having a memory. The process requires the entry of data corresponding to coefficients C_1, C_2, C_3, as well as time periods τ_p (initial time delay after drug infusion) and T_p (time constant representing speed of response) to be entered into the memory of the computing machine. As such, this is a 35 U.S.C. § 101 process that is "... tied to another statutory class ... ," and therefore complies with the discussion on Interim Guidelines set forth in the Memorandum of May 15, 2008 from John J. Love, Deputy Commissioner for Patent Examination Policy, to the Technology Center Directors. Specifically, the process of amended independent claim 1 is tied to the statutory machine class of 35 U.S.C. § 101. Dependent claims 2, 3, 5 and 6 depend from amended independent claims 1 and 4, and have been correspondingly similarly amended.

In view of the foregoing, it is respectfully asserted that the Examiner's rejection of claims 1-6 under 35 U.S.C. § 101 has been overcome.

With respect to independent claim 7, this claim has been amended to specify with greater precision that the claimed subject matter corresponds to "apparatus," rather than a "system."

Independent claim 4 has been amended to state the statutory machine class of 35 U.S.C. § 101 with greater specificity. More specifically, the preamble of this apparatus claim has been amended to identify the claimed subject matter as "apparatus," rather than a "system."

In view of the foregoing, the Examiner's rejection of claims 1-10 under 35 U.S.C. § 101 is believed to have been overcome.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 7-10 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to point out with particularity and claim distinctly the subject matter that Applicants regard as the invention. According to the Examiner, the metes and the bounds of the claimed structure can not be determined by the disclosure.

The Examiner states that Applicants have claimed a signal combiner, a limiter, and the virtual anesthesia monitor. However, it is unclear to the Examiner if the claimed signal combiner, limiter and virtual anesthesia monitor are structures, or algorithms, or software (data structures). If the determination means is an algorithm or software then the term/limitation will not be given patentable weight because it lacks structure that would be attributed to the apparatus claims.

The Examiner notes that the word "for" in the claims can may be interpreted as intended use. Intended use/functional language does not, according to the Examiner, require that a reference specifically teach the intended use of the element. A recitation of the intended use of the claimed invention must, according to the Examiner, result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention

from the prior art. If the prior art structure is capable of performing the intended use then, according to the Examiner, it meets the claim.

<u>APPLICANTS' RESPONSE</u>

Applicants respectfully disagree with the Examiner's contention that algorithms and data structures in the present case are not entitled to patentable weight. Moreover, it is respectfully further asserted that the Examiner incorrectly contends that these elements would "[lack] structure that would be attributed to ... apparatus claims."

In regard of the foregoing it is noted that independent claim 7 has since the time of filing of the present case specified its claimed subject matter in the context of a "system," that contains elements that unquestionably constitute apparatus. These include, for example, the first, second, and third memories. The remaining elements, specifically the signal combiner arrangement, the limiter, and the virtual anesthesia monitor, are described in the present application at, for example, Fig. 1, which shows a plurality of signals being combined in a computer, and in corresponding portions of the specification (*e.g.*, page 5, lines 5-16). It is evident from the figures and the specification that these elements, *i.e.*, the signal combiner arrangement, the limiter, and the virtual anesthesia monitor, as well as the limiter, are implemented in a computer. It is well-established that a computer is a machine that assumes machine characteristics that are responsive to the program it is running.

In the present case, the claimed elements identified by the Examiner are not merely algorithms or data structures, but instead constitute machine elements having every characteristic of apparatus. Accordingly, for these and other reasons, it is respectfully asserted that the metes and bounds of these elements can readily be determined from the specification and drawings, and accordingly, the rejection of claims 7-10 by the Examiner under 35 U.S.C. § 112, second paragraph, has been traversed.

The foregoing notwithstanding, Applicants have amended claims 7-10 to specify the subject matter therein claimed as "apparatus," which clearly is a statutory class, the claimed combination of elements being entitled to patentable weight.

Claim Rejections - 35 U.S.C. § 102(b)

Claims 1-10 stand rejected under 35 U.S.C. § 102(b) as specifying subject matter considered by the Examiner to be anticipated by Kangas, *et al.* (US 5,775,330) herein after referred as Kangas, *et al.*

Regarding claims 1-6, the Kangas, *et al.* reference is considered by the Examiner to disclose a method of predicting the anesthetic depth of a person by analyzing his EEG signals (claim 1).

Regarding claims 7-10, the Kangas, *et al.* reference is considered by the Examiner to disclose an apparatus that recodes the data (column 7, lines 3-37), process the EEG signals and transforms them to predict the anesthetic depth of a patient (claim 13). The invention of the Kangas, *et al.* reference includes a memory that is used to record data during surgery for seven different subjects (column 7, lines 3-9).

APPLICANTS' RESPONSE

Briefly, the Kangas, *et al.* reference describes a method and apparatus for collecting EEG data, reducing the EEG data into coefficients, and correlating those coefficients with a depth of unconsciousness or anesthetic depth, and which obtains a bounded first derivative of anesthetic depth to indicate trends. An artificial neural network based method continuously analyzes EEG data to discriminate between awake and anesthetized states in an individual and continuously monitors anesthetic depth trends in real-time. This enables an anesthesiologist to respond to changes in anesthetic depth of the patient during surgery and to administer the correct amount of anesthetic. The use of brain wave data processed by a trained neural network ascertains the

level of consciousness of an individual and a consciousness trend before during and after exposure to anesthetic.

The foregoing notwithstanding, the system described in the Kangas, *et al.* reference cannot determine whether the patient is adequately anesthetized. The adequacy of anesthesia is a difficult problem for anesthesiologists who occasionally fail despite the fact that they attempt to over anesthetize the patient to ensure adequate anesthesia.

The Kangas, *et al.* reference is directed to anesthesia depth measurement and calculation only. The word "prediction" is used in regard of the known system only in the sense that EEG signals are "analyzed" to "calculate" anesthesia depth and its derivatives. This known system, however, does not address the issue of how a drug input strategy will influence the anesthesia depth in the future. On the contrary, the present claimed invention achieves drug impact prediction. The system of the Kangas, *et al.* reference does not possess a "prediction" capability, as does the present invention, but rather is a method of calculating actual (not predicted) anesthesia depth. In short, the Kangas, *et al.* reference teaches subject matter already in use in FDA approved devices, such as the BIS Monitor by Aspect, and Entropy Monitor by GE, which are employed for anesthesia depth measurements and which produce a corresponding display to the operator. In contrast, anesthesia depth measurements are the input signals to the present claimed system.

In addition to the foregoing, it is noted that drug impact prediction depends on the response to drugs by each individual patient. Thus, there is a need for individual patient dynamic models. The system described in the Kangas, *et al.* reference has nothing to do with patient models. In fact, it is admitted in the Kangas, *et al.* reference that the invention therein described cannot determine whether the patient is adequately anesthetized. It is therefore respectfully asserted that the Examiner has incorrectly characterized the Kangas, *et al.* reference as

"predicting the anesthetic depth of a person by analyzing his EEG signals" or as useful to "process the EEG signals and transform them to predict the anesthetic depth of a patient."

With reference to amended independent claim 1, it is noted that this claim specifies a "method of using a computing machine having a memory to assist a human expert in reducing predictable variations in the depth of anesthesia during the administration of a medical anesthesia drug to a patient." Nothing in the Kangas, *et al.* reference achieves, teaches, or suggests such prediction.

With reference to amended independent claim 4, it is noted that this claim specifies a "method of using a computing machine having a memory to determine a model that corresponds to a predicted response of a patient to anesthesia drug delivery." Nothing in the Kangas, *et al.* reference teaches or suggests the determination of a model of a patient response, or a prediction of the patient's response to anesthesia.

With respect to amended independent claim 7, it is noted that this claim specifies "apparatus for determining a predicted response of a patient to the administration of an anesthesia drug." Again, nothing in the Kangas, *et al.* reference teaches or suggests the predicting of a patient's response to anesthesia.

In view of the foregoing, it is respectfully asserted that the Examiner's rejection of claims 1-10 under 35 U.S.C. § 102(b) has been overcome, and that these claims are in allowable condition.

Prior Art Cited But Not Applied

The prior art made of record and not relied upon is considered by the Examiner to be pertinent to Applicants' disclosure. In this regard, the Examiner cited the following references as disclosing related limitations of the applicant's claimed and disclosed invention.

Nomura; Takashi, *et al.* (US 5964713 A), is considered by the Examiner to disclose a method and apparatus to predict the anesthetic depth of a patient undergoing surgery. Briefly,

this reference discloses a system that achieves only anesthesia depth measurement and calculation. The word "prediction" is used only in the sense that it can "analyze" body signals (such as blood pressures, body temperature, and respiratory rates) to "calculate" anesthesia depth. The known system does not address the issue of how a drug input strategy will influence the anesthesia depth in the future. Thus, this known arrangement is not capable of generating a "prediction," but instead is a method of calculating anesthesia depth. In addition, the subject matter of this reference teaches nothing regarding patient models.

Tang; Sharon S., *et al.* (US 6658396 B1), is considered by the Examiner to disclose an apparatus for predicting the optimal dosage for a particular patient while considering a plurality of factors.

In this known arrangement, a computerized neural network drug dosage estimator predicts what will happen when a patient, or a patient population, is administered a drug dosage deviating from predicted optimal dosage. For example, if an individual patient of certain characteristics does not exhibit desired therapeutic response at a certain (possibly even the predicted optimal) drug dosage level, then the question arises whether the dosage should be increased by 10%, or by 25%, or by 50%, or even by 100%? The neural network drug dosage estimator of the Tang, *et al.* reference helps to answer this question.

The known arrangement is embodied in a computerized method of predicting an optimal dosage of a particular drug for a particular patient in consideration of previously determined optimal dosages of the drug for members of a patient population. More particularly, the known system requires that a neural network having an architecture of one or more slabs be programmed. The slabs collectively relate "input data" to "output data". The "input data" includes at least a selected three (3) of a person's traits drawn from at least two (2) of the three (3) groups of information, specifically:

Group 1 overt indications of (1a) age, (1b) gender, (1c) race, (1d) ethnicity, (1e) diet type, (1f) height, (1g) weight, and (1h) body surface area;

Group 2 medical diagnostic indications of (2a) blood pressure, (2b) use of a drug other than the particular drug at the same time as use of the particular drug, (2c) fitness, (2d) peptide levels, and (2e) genetic predisposition to a particular disease; and

Group 3 pharmacological indications of (3a) pharmacokinetic parameters, (3b) pharmacodynamic parameters.

The number and diversity of traits quantitatively distinguish the system described in the Tang, *et al.* reference over systems that employ a family of curves relating recommended dosage by age, weight and sex *(i.e.*, by three traits). The "output data" is the clinically-determined optimal drug dosage for the same person.

The system described in the Tang, *et al.* reference is quite complex, as it uses neural network models that inevitably require determination of a large number of model parameters. They require a large and very rich data set for training and tuning. Consequently, they cannot be established in real-time during surgical procedures. The present invention, on the other hand, utilizes only a very small number of parameters that are computationally feasible to be established in real time during anesthesia procedures.

A further advantage of the present invention over that described in the Tang, *et al.* reference is the interaction of the model with physicians. More specifically, model parameters in neural networks do not carry any physiological meaning. Consequently, they cannot be communicated to physicians. The system of the present invention uses parameters derived from anesthesiologists' viewpoints of anesthesia depth responses, and hence they have direct and clear physiological meanings, such as time delay, response speed, drug sensitivity. They allow physicians to understand the model operation, to set safety bounds of parameters, and to calibrate. The elements of the claims of the present invention relate directly to such parameters.

A still further advantage of the present invention over the system described in the Tang, *et al.* reference relates to the data sets needed for establishing the models. In the known arrangement, the models must be learned and tuned by using large population data. As stated in the Tang, *et al.* patent "the number of cases required to train the neural network is on the order of a minimum of 500 to 2,000, and more commonly 10,000." To establish an individual patient's model, only one patient's data in one anesthesia procedure can be used. More specifically, the inventive system establishes a patient's unique dynamic model in real-time, without any requirements from other patients' models.

Yet another advantage of the present invention over the system of the Tang, *et al.* reference relates to real-time and individualized patient models. Drug impact prediction depends on each individual patient's response to drugs, hence requires individual patient's dynamic models. The system of the Tang, *et al.* reference uses models that are established by using large data sets from a large patient population (such as 10000 cases). Hence, they constitute average population models, not real prediction for an individual but rather guesses of most probable outcomes based on population studies of large numbers of patients. Large variations in patient dynamics and drug responses make population-based average models unusable for real-time anesthesia depth prediction, control, and management. In other words, the system of the Tang, *et al.* reference cannot be used to derive an individual patient's model using real-time data in one anesthesia procedure.

In view of the foregoing, neither the Nomura, *et al.* nor Tang, *et al.* references teach or suggest the claimed invention.

Conclusion

In view of the foregoing, it is respectfully requested that the Examiner reconsider the present application, allow the claims, and pass the application for issue. If the Examiner believes

that the prosecution of this case can be expedited by a telephone interview, the Examiner is requested to call attorney for Applicant(s) at the telephone number indicated hereinbelow.

Respectfully submitted,

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RAM:rb:ROA-d01.WSL

enc Annexure 1 - Claims Rewritten to Show Amendments
Annexure 2 - Specification Rewritten to Show Amendments
Annexure 3 - Replacement Sheets of Drawing Figures (12 sheets)
File: ROA-d01.WSL